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Date July 21, 2003

To Examiner S. Devi, Ph.D.
U.S. Patent and Trademark Office (Patent)
Commissioner for Patents
Washington, D.C. 20231
Telephone: 703-308-9347

Facsimile number 08919-02200001 / 703-~~305-3014~~ 308-4556

From Y. Rocky Tsao

Re PEPTIDE REPEAT IMMUNOGENS
Applicant: Jaulang Hwang et al.
Application No.: 09/412,558
Filing Date: October 5, 1999
Country: United States
Your Ref.: 13A-880115
Our Ref.: 08919-022001

Number of pages including this page 3

Message

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1859-1951

July 19, 2003

S. Devi, Ph.D.
U.S. Patent and Trademark Office (Patent)
Commissioner for Patents
Washington, D.C. 20231

Re: PEPTIDE REPEAT IMMUNOGENS
Your Ref.: 13A-880115
Our Ref.: 08919-022001

Dear Examiner Devi:

FR

BOSTON
DALLAS
DELAWARE
NEW YORK
SAN DIEGO
SILICON VALLEY
TWIN CITIES
WASHINGTON, DC

Thank you for granting a telephone interview, scheduled for 2:00 pm July 21, 2003 to discuss issues raised in the final office action and the advisory action. This letter, limited to claims 14 and 24 to facilitate discussion, outlines what we would like to discuss with you during the interview.

Rejection under 35 U.S.C. § 112, first paragraph

Claim 24, rejected for containing new matter, is drawn to a nucleic acid encoding a polypeptide having (1) the receptor binding domain of a *Pseudomonas exotoxin* A (PE) and (2) at least two copies of an antigenic peptide sequence, and excludes the non-receptor binding domain of the PE. You contended that the recitation "excludes the non-receptor binding domain of the *Pseudomonas exotoxin* A" constitutes new matter. We disagree.

The specification has taught a plasmid pPEDIG12, which encodes a fusion polypeptide of domain Ia of PE (the receptor binding domain) and 12 repeats of GnRH. See page 10, lines 12-16 in the specification. The sequence encoding the former is from plasmid pJH14 disclosed in Hwang et al. (J. Biol. Chem. 264:2379-2384, 1989). Note that pJH14 encodes a polypeptide containing only domain Ia and excluding any other domains of PE (i.e., non-receptor domains). See page 2380, Fig. 1A. In other words, pPEDIG12 encodes a polypeptide that also excludes the non-receptor binding domain. Thus, the recitation at issue does not contain new matter.

Rejection under 35 U.S.C. § 102

1. You maintained the rejection against claim 14 as being anticipated by Lorberboum-Galski, as evidenced by Burnie. See the final office action, page 4, part 12.

Claim 14 covers a nucleic acid encoding a polypeptide that contains (1) the receptor binding domain of a PE, and (2) at least three copies of an antigenic peptide sequence. It is well known in the art that an antigenic peptide contains at least one epitope. An epitope has a stable spatial conformation so that it can stimulate the immune system to generate specific antibodies that recognize its stable spatial conformation. Lorberboum-Galski discloses a DNA sequence encoding a polypeptide including the full-length PE and 1 to 3 copies of "flexible" linker sequence of GGGGS. See column 2, lines 56-59. As the linker is flexible, i.e., unstable, it is not antigenic. Thus, Lorberboum-Galski does not anticipate claim 14.

2. You also rejected claim 14 as being anticipated by Hickey. See the final office action, part 13. Hickey teaches GnRH-PE conjugates, as well as GnRH-PE chimeric hybrid proteins prepared by the recombinant DNA technology. As the GnRH-PE chimeric hybrid proteins have two copies of

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GnRH (see page 9, lines 29-32), they differs from that encoded by the nucleic acid of claim 14, which has at least three copies of an antigenic peptide sequence.

Referring to page 13 of Hickey, you concluded that Hickey teaches an immunogenic system containing 2-20 GnRH's, and therefore anticipated claim 14. See the advisory action, page 5, lines 1-3. The Hickey immunogenic system is a branched polymer. It differs from the linear polypeptide encoded by the nuclei acid of claim 14. Clearly, your conclusion is based on a factually erroneous premise.

Rejection under 35 U.S.C. § 103(a)
You rejected claim 24 as being unpatentable over Hickey in view of Hwang and Pastan. See the final office action, pages 5-7, part 14.

As discussed in our response to the final office action, the three cited references would not have motivated one skilled in the art to combine their teachings. Indeed, Hickey teaches using PE as an immunogenic carrier. In particular, it teaches that "preferred Pseudomonas exotoxin variants are [those] having decreased toxicity ... having amino acids 1-252 (domain Ia) deleted." See, e.g., the paragraph bridging pages 9 and 10. Pastan teaches that "PE molecules with a deletion of Domain Ia are effective immunotoxins with diminished side effects ..." See column 3, lines 15-18. To the extent that these two references point out side effects of domain Ia, they both teach away using this domain in an immunogenic carrier. Of note, Hwang teaches that domain Ia can be used as an antigen for producing vaccines against PE but not an immunogenic carrier as taught in Hickey. Thus, the 3 references, alone or combined, would not have motivated one skilled in the art to combine their teachings and do not render claim 24 obvious.

In the advisory action, you asserted that the response was not persuasive, as claim 24 was not drawn to an immunization method. The issue here is whether the cited references would have motivated one skilled in the art to make a nucleic acid of claim 24, which encodes a polypeptide having domain Ia and an antigenic sequence. For the reasons set forth above, they clearly would not have.

We look forward to discussing with you the above issues at the interview and others on July 21. To expedite the prosecution, we would like to invite your supervisor to this interview. If you agree, please provide a copy of this letter to him before the interview.

Very truly yours,

Y. Rocky Tsao

Y. Rocky Tsao, Ph.D., J.D.
Reg. No. 34,053

3:23:30